

WHAT IS CLAIMED IS:

1. A method of defining the portion of one or more chemical compounds having binding affinity for a target receptor comprising:
 - (a) identifying one or more key component fragments of one or more chemical compounds having binding affinity for a target receptor;
 - (b) coupling one or more analogs of the one or more chemical compounds to a carrier molecule to construct one or more analog-carrier conjugates, said analogs containing one or more of the key component fragments, said analog being coupled to the carrier such that one or more of the key component fragments are exposed;
 - (c) utilizing the analog-carrier conjugates to generate monoclonal antibodies *in vivo* or *in vitro* that are able to define the exposed key component fragments; and
 - (d) determining the monoclonal antibodies which are most specific for the key component fragments of the one or more chemical compounds and which bind to the one or more chemical compounds.
2. The method of claim 1 wherein the ability of the monoclonal antibodies to mimic the binding site of a target receptor is determined.
3. The method of claim 1, wherein two or more analogs are utilized to generate a panel of monoclonal antibodies, and wherein each analog-carrier conjugate defines a key component fragment of the one or more chemical compounds, and wherein the analog-carrier conjugates together define all of the key component fragments of the one or more chemical compounds.

4. The method of claim 3, wherein each member of the panel of monoclonal antibodies binds specifically to a portion of the one or more chemical compounds.

5. The method of claim 1, wherein two or more analogs are utilized to generate a panel of monoclonal antibodies, wherein two or more carrier conjugates defines a key component fragment of the one or more chemical compounds, and wherein the analog-carrier conjugates together define a portion of the entire surface conformation of the one or more chemical compounds.

6. The method of claim 1, wherein the monoclonal antibodies generated for each analog are tested for their dissociation constant, and those exhibiting the strongest binding are included in a panel such that each different analog is represented by monoclonal antibodies in the panel.

7. The method of claim 6, wherein the dissociation constant is in the range of from about 0.01 nM to about 10nM.

8. The method of claim 1, wherein the monoclonal antibodies are generated using *in vivo* immunization methods.

9. The method of claim 1, wherein the monoclonal antibodies are generated using *in vitro* immunization methods.

10. The method of claim 1, wherein the carrier molecule is selected from the group consisting of Keyhole Limpet Hemocyanin, ovalbumin and thyroglobulin.

11. The method of claim 1, wherein the one or more chemical compounds exhibit PDEIV inhibitor or opiate activity.

12. The method of claim 1, wherein the functional groups are selected from the group consisting of carboxyl, hydroxyl, keto, amino, nitro, and sulfhydryl.
13. The method of claim 1, wherein the one or more chemical compounds identified are organic molecules.
14. The method of claim 1, wherein the one or more chemical compounds identified are inorganic molecules.
15. The method of claim 1, wherein the one or more chemical compounds identified are biological molecules.
16. The method of claim 1, wherein the one or more chemical compounds having binding affinity for a target receptor have a molecular weight of less than approximately 1000 g/mole.
17. The method of claim 1, wherein the one or more chemical compounds having binding affinity for a target receptor have a molecular weight of less than approximately 500 g/mole.
18. The method of claim 1, wherein the panel of monoclonal antibodies is comprised of 2-3 monoclonal antibodies.
19. The method of claim 1, wherein the analogs either (i) contain at least one functional group allowing attachment of the analog to the carrier molecule; or (ii) are modified to contain at least one functional group allowing attachment of the analog to the carrier molecule
20. The method of claim 1, further comprising verifying that additional small molecules are part of the structural class to which the compound that generically defines the surface

conformation and surface charge density belongs.

21. The method of claim 1, wherein a three-dimensional structure of the antigen binding region of one or more of the monoclonal antibodies is determined.

22. The method of claim 21, wherein the three-dimensional structure of the antigen binding region is used to design new molecules.

23. The method of claim 21, wherein the three-dimensional structure of the antigen binding region is used to evaluate the exterior molecular characteristics of one or more compounds of interest to determine whether the compounds of interest have binding affinity for the target receptor.

24. A method of identifying compounds which have binding affinity for a target receptor comprising:

(a) identifying one or more key component fragments of one or more chemical compounds having binding affinity for a target receptor;

(b) coupling one or more analogs of the one or more chemical compounds to a carrier molecule to construct one or more analog-carrier conjugates, said analogs containing one or more of the key component fragments, said analog being coupled to the carrier such that one or more of the key component fragments are exposed;

(c) utilizing the analog-carrier conjugates to generate monoclonal antibodies *in vivo* or *in vitro* that are able to define the exposed key component fragments; and

(d) determining the monoclonal antibodies which are most specific for the key component fragments of the one or more chemical compounds and which bind to the one or more

chemical compounds;

(e) immobilizing the monoclonal antibodies on a support; and

(f) conducting a series of assays utilizing said immobilized monoclonal antibodies to screen one or more compounds of interest.

25. The method of claim 24, wherein the ability of the monoclonal antibodies to mimic the binding site of a target receptor is determined.

26. The method of claim 24, wherein two or more analogs are utilized to generate a panel of monoclonal antibodies, and wherein, each analog-carrier conjugate defines a key component fragment of the one or more chemical compounds, and wherein the analog-carrier conjugates together define all of the key component fragments of the one or more chemical compounds.

27. The method of claim 24, wherein two or more analogs are utilized to generate a panel of monoclonal antibodies, and wherein each analog-carrier conjugate defines a key component fragment of the one or more chemical compounds, and wherein the analog-carrier conjugates together define a portion of the entire surface conformation of the one or more chemical compounds.

28. The method of claim 24, wherein the monoclonal antibodies generated for each analog are tested for their dissociation constant and those exhibiting the strongest binding are included in a panel such that each different analog is represented by monoclonal antibodies in the panel.

29. The method of claim 28, wherein the dissociation constant is in the range from about 0.01 nM to about 10 nM.

30. The method of claim 24, wherein the monoclonal antibodies are generated using *in vivo* immunization methods.
31. The method of claim 24, wherein the monoclonal antibodies are generated using *in vitro* immunization methods.
32. The method of claim 24, wherein the functional groups are selected from the group consisting of carboxyl, hydroxyl, keto, amino, nitro, and sulfhydryl.
33. The method of claim 24, wherein the one or more compounds of interest are obtained from 1) combinatorial libraries of peptides, synthetic ethers, or phosphonates; 2) natural product extracts; 3) microbial or other cell culture broths; 4) synthetic products; 5) synthetic analogs; 6) intermediates of drug candidates or drug metabolites.
34. The method of claim 24, wherein the carrier molecule is selected from the group consisting of Keyhole Limpet Hemocyanin, ovalbumin and thyroglobulin.
35. The method of claim 24, wherein the one or more chemical compounds exhibit PDEIV inhibitor or opiate activity.
36. The method of claim 24, wherein the panel of monoclonal antibodies is pooled before attachment to the support.
37. The method of claim 24, wherein each member of the panel of monoclonal antibodies is utilized separately to screen compounds of interest.
38. The method of claim 24, wherein the one or more chemical compounds are organic molecules.

39. The method of claim 24, wherein the one or more chemical compounds having binding affinity for a target receptor have a molecular weight of less than approximately 1000 g/mole.

40. The method of claim 24, wherein the one or more chemical compounds having binding affinity for a target receptor have a molecular weight of less than approximately 500 g/mole.

41. The method of claim 24, wherein the one or more chemical compounds identified are inorganic molecules.

42. The method of claim 24, wherein the one or more chemical compounds identified are biological molecules.

43. The method of claim 24, wherein the panel of monoclonal antibodies is comprised of 2-3 monoclonal antibodies.

44. A method of defining a portion of one or more PDEIV inhibitors comprising:

(a) identifying one or more key component fragments of one or more PDEIV inhibitors;

(b) coupling one or more analogs of the one or more PDEIV inhibitors to construct one or more analog-carrier conjugates, said analogs containing one or more of the key component fragments, said analogs being coupled to the carrier such that one or more of the key component fragments are exposed;

(c) utilizing the analog-carrier conjugates to generate monoclonal antibodies *in vivo* or *in vitro* that define the exposed key component fragments; and

(d) determining the antibodies which are most specific for the key component fragments of the one or more PDEIV inhibitors and which bind to the one or more PDEIV inhibitors.

45. The method of claim 44, wherein the key component fragments are derived from 3-(3-cyclopentyloxy-4-methoxybenzyl)-6-ethylamino-8-isopropyl-3H-purine.

46. The method of claim 44, wherein the analogs that may be attached to the carrier molecule are 3-(3-cyclopentyloxy-4-methoxybenzyl)-6-amino-8-isopropyl-purine and 6-ethylamino-8-isopropyl-3-(p-aminomethylphenyl)-purine.

47. The method of claim 44, wherein the analogs that may be attached to the carrier molecule are rolipram, 3-(3-cyclopentyloxy-4-methoxybenzyl)-6-ethylamino-8-isopropyl-purine or RP73401, wherein the analogs are attached via an ether linkage from the 4-O to the carrier molecule.

48. The method of claim 44, wherein the key component fragments are derived from 3,5-di-t-butyl-4-hydroxy-benzyl-5-chloro-2-(2-pyridyl)-ethynyl-benzoxazole.

49. A method of identifying compounds which inhibit PDEIV comprising:

(a) identifying one or more key component fragments of one or more PDEIV inhibitors;

(b) coupling one or more analogs of the one or more PDEIV inhibitors to a carrier molecule to construct one or more analog-carrier conjugates, said analogs containing one or more of the key component fragments, said analog being coupled to the carrier such that one or more of the key component fragments are exposed;

- (c) utilizing the analog-carrier conjugates to generate monoclonal antibodies *in vivo* or *in vitro* that are able to define the exposed key component fragments; and
- (d) determining the monoclonal antibodies which are most specific for the key component fragments of the one or more chemical compounds and which bind to the one or more PDEIV inhibitors;
- (e) immobilizing the monoclonal antibodies on a support; and
- (f) conducting a series of assays utilizing said immobilized monoclonal antibodies to screen one or more compounds of interest.

50. The method of claim 49, wherein the key component fragments are derived from 3-(3-cyclopentyloxy-4-methoxybenzyl)-6-ethylamino-8-isopropyl-purine.

51. The method of claim 49, wherein the analogs that may be attached to the carrier molecule are 3-(3-cyclopentyloxy-4-methoxybenzyl)-6-amino-8-isopropyl-purine and 6-ethylamino-8-isopropyl-3-(p-aminomethylphenyl)-purine.

52. The method of claim 49, wherein the analogs that may be attached to the carrier are rolipram, 3-(3-cyclopentyloxy-4-methoxybenzyl)-6-ethylamino-8-isopropyl-purine or RP73401, wherein the analogs are attached via an ether linkage from the 4-O to the carrier molecule.

53. The method of claim 49, wherein the key component fragments are derived from 3,5-di-t-butyl-4-hydroxy-benzyl-5-chloro-2-(2-pyridyl)-ethynyl-benzoxazole.

54. A method of designing molecules possessing defined exterior molecular characteristics comprising:

- (a) identifying one or more key component fragments of one or more chemical compounds having binding affinity for a target receptor;
- (b) coupling one or more analogs of the one or more chemical compounds to a carrier molecule to construct one or more analog-carrier, said analogs containing one or more of the key component fragments, said analog being coupled to the carrier such that one or more of the key component fragments are exposed;
- (c) utilizing the analog-carrier conjugates to generate monoclonal antibodies *in vivo* or *in vitro* that are able to define the exposed key component fragments; and
- (d) determining the monoclonal antibodies which are most specific for the key component fragments of the one or more chemical compounds and which bind to the one or more chemical compounds;
- (e) immunizing an animal with the monoclonal antibodies to generate anti-idiotypic monoclonal antibodies reactive against the antigen binding region of the immunizing monoclonal antibodies; and
- (f) determining a three-dimensional structure of the antigen binding region of the anti-idiotypic antibodies.

55. The method of claim 54, wherein the three-dimensional structure of the antigen binding region is used to design new molecules.

56. The method of claim 54, wherein the three-dimensional structure of the antigen binding region is used to evaluate the exterior molecular characteristics of one or more compounds of interest to determine whether the compounds of interest have binding affinity for the target receptor.

57. The method of claim 54, further comprising testing the anti-idiotypic monoclonal antibodies to determine whether the anti-idiotypic monoclonal antibodies bind to the target receptor.

58. The method of claim 58, further comprising generating anti-anti-idiotypic antibodies with binding specificity for the anti-idiotypic monoclonal antibody antigen binding region.

59. The method of claim 58, further comprising determining the ability of the anti-anti-idiotypic monoclonal antibody to bind to the one or more chemical compounds having binding affinity for the target receptor.

60. The method of claim 54, wherein the carrier molecule is selected from the group consisting of Keyhole Limpet Hemocyanin, ovalbumin and thyroglobulin.

61. The method of claim 54, wherein the one or more chemical compounds exhibits PDEIV inhibitor or opiate activity.

62. The method of claim 54, wherein the functional groups are selected from the group consisting of carboxyl, hydroxyl, keto, amino, nitro, and sulfhydryl.

63. The method of claim 44 wherein the ability of the monoclonal antibodies to mimic the binding site of PDEIV is determined.

64. The method of claim 44, wherein two or more analogs are utilized to generate a panel of monoclonal antibodies, and wherein each analog-carrier conjugate defines a key component fragment of the one or more PDEIV inhibitors, wherein the analog-carrier conjugates together define all of the key component fragments of the one or more PDEIV inhibitors.

65. The method of claim 64, wherein each member of the panel of monoclonal antibodies binds specifically to a portion of the one or more PDEIV inhibitors.

66. The method of claim 44, wherein two or more analogs are utilized to generate a panel of monoclonal antibodies, wherein two or more carrier conjugates defines a key component fragment of the one or more PDEIV inhibitors, and wherein the analog-carrier conjugates together define a portion of the entire surface conformation of the one or more PDEIV inhibitors.

67. The method of claim 44, wherein the monoclonal antibodies generated for each analog are tested for their dissociation constant, and those exhibiting the strongest binding are included in a panel such that each different analog is represented by monoclonal antibodies in the panel.

68. The method of claim 67, wherein the dissociation constant is in the range of from about 0.01 nM to about 10nM.

69. The method of claim 44, wherein the monoclonal antibodies are generated using *in vivo* immunization methods.

70. The method of claim 44, wherein the monoclonal antibodies are generated using *in vitro* immunization methods.

71. The method of claim 44, further comprising verifying that additional small molecules are part of the structural class to which the compound that generically defines the surface conformation and surface charge density belongs.

72. The method of claim 44, wherein a three-dimensional structure of the antigen binding region of one or more of the monoclonal antibodies is determined.

73. The method of claim 72, wherein the three-dimensional structure of the antigen binding region is used to design new molecules.

74. The method of claim 72, wherein the three-dimensional structure of the antigen binding region is used to evaluate the exterior molecular characteristics of one or more compounds of interest to determine whether the compounds of interest have binding affinity for the target receptor.

75. The method of claim 1, wherein the carrier molecule is selected from the group consisting of Keyhole Limpet Hemocyanin, ovalbumin and thyroglobulin

76. The method of claim 1, wherein the functional groups are selected from the group consisting of carboxyl, hydroxyl, keto, amino, nitro, and sulfhydryl.

77. The method of claim 1, wherein the panel of monoclonal antibodies is comprised of 2-3 monoclonal antibodies.

78. The method of claim 1, wherein the analogs either (i) contain at least one functional group allowing attachment of the analog to the carrier molecule; or (ii) are modified to contain at least one functional group allowing attachment of the analog to the carrier molecule

79. The method of claim 49, wherein the ability of the monoclonal antibodies to mimic the binding site of PDEIV is determined.

80. The method of claim 49, wherein two or more analogs are utilized to generate a panel of monoclonal antibodies, and wherein, each analog-carrier conjugate defines a key component fragment of the one or more PDEIV inhibitors, and wherein the analog-carrier conjugates together define all of the key component fragments of the PDEIV inhibitors.

81. The method of claim 49, wherein two or more analogs are utilized to generate a panel of monoclonal antibodies, and wherein each analog-carrier conjugate defines a key component fragment of the one or more PDEIV inhibitors, and wherein the analog-carrier conjugates together define a portion of the entire surface conformation of the one or more PDEIV inhibitors.

82. The method of claim 49, wherein the monoclonal antibodies generated for each analog are tested for their dissociation constant and those exhibiting the strongest binding are included in a panel such that each different analog is represented by monoclonal antibodies in the panel.

83. The method of claim 82, wherein the dissociation constant is in the range from about 0.01 nM to about 10 nM.

84. The method of claim 49, wherein the monoclonal antibodies are generated using *in vivo* immunization methods.

85. The method of claim 49, wherein the monoclonal antibodies are generated using *in vitro* immunization methods.

86. The method of claim 49, wherein the functional groups are selected from the group consisting of carboxyl, hydroxyl, keto, amino, nitro, and sulfhydryl.

87. The method of claim 49, wherein the one or more compounds of interest are obtained from 1) combinatorial libraries of peptides, synthetic ethers, carbohydrates or phosphonates; 2) natural product extracts; 3) microbial or other cell culture broths; 4) synthetic products; 5) synthetic analogs; 6) intermediates of drug candidates or drug metabolites.

88. The method of claim 49, wherein the carrier molecule is selected from the group consisting of Keyhole Limpet Hemocyanin, ovalbumin and thyroglobulin.

89. The method of claim 49, wherein the panel of monoclonal antibodies is pooled before attachment to the support.

90. The method of claim 49, wherein each member of the panel of monoclonal antibodies is utilized separately to screen compounds of interest.

91. The method of claim 49, wherein the panel of monoclonal antibodies is comprised of 2-3 monoclonal antibodies.